



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/077,065	02/15/2002	Venita I. DeAlmeida	P1872R1	3480

7590 04/07/2005

DENISE M. KETTELBERGER, Ph.D
P.O. BOX 2903
MINNEAPOLIS, MN 55402-0903

EXAMINER

EWOLDT, GERALD R

ART UNIT	PAPER NUMBER
----------	--------------

1644

DATE MAILED: 04/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/077,065

Applicant(s)

DEALMEIDA ET AL.

Examiner

G. R. Ewoldt, Ph.D.

Art Unit

1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 February 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-52 is/are pending in the application.
- 4a) Of the above claim(s) 10-41 and 46-52 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-9 and 42-45 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

Art Unit: 1644

DETAILED ACTION

1. Applicant's election of Group I, Claims 1-9 and 42-45, filed 2/22/05, without traverse, is acknowledged.
2. Claims 10-41 and 46-52 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b).

Claims 1-9 and 42-45 are pending and under examination.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-9 and 42-45 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, the specification provides insufficient evidence that the claimed method could be used to effectively treat insulin resistance or hypoinsulinemia, or be used to repair or regenerate muscle in a mammal.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention, *in re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

Regarding novel methods involving biological processes, "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The "amount of guidance or direction" refers to that information in

Art Unit: 1644

the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling (MPEP 2164.03)". The MPEP further states that physiological activity can be considered inherently unpredictable. The state of the medical arts are such that essentially nothing is known regarding the use of Dkk-1 antagonists for the treatment of insulin resistance or hypoinsulinemia, or the repair or regeneration of muscle.

The method of the instant claims presumably functions by employing an antagonist of Dkk-1, such as an antibody, such that Dkk-1 is unavailable for the downregulation of Wnt family proteins. Thus, it is actually the upregulation (or lack of downregulation) of Wnt proteins that would provide the treatment of insulin resistance or hypoinsulinemia, or the repair or regeneration of muscle. The specification implies that Wnt proteins activate numerous other proteins involved in the insulin-signaling cascade or the differentiation of myocytes into adipocytes. Presumably, upregulating Wnt proteins would upregulate downstream effectors leading to increased insulin metabolism and decreased differentiation of myocytes into adipocytes (which would presumably result in the repair or regeneration of muscle).

A review of the specification discloses just a single relevant example (Example 1) supporting the method of the instant claims. The example discloses that the culture of L6 myoblasts in a medium including Dkk-1 causes reduced insulin-stimulated glucose uptake, while the culture of 3T3/L1 fibroblasts in a medium including Dkk-1 causes increased insulin-stimulated glucose uptake and the decrease in the expression of some markers that would indicate adipocyte differentiation in said cells. The disclosure also teaches that the injection of Dkk-1 into mice causes altered expression of muscle specific genes and reduces insulin secretion, and that overexpression of *dkk-1* in transgenic mice causes reduced size and bodyweight in the animals. It is unclear how this disclosure is intended to enable the method of the instant claims.

Art Unit: 1644

The specification fails to disclose that, like many developmental genes, Wnt family genes are both developmental genes and proto-oncogenes (see for example, Behrens et al. 2004). As taught by LeFloch et al. (2005), "Inappropriate expression of Wnt/APC/ β -catenin signaling pathways plays a critical role at the early stages in a variety of human cancers". Uematsu et al. (2003) "identified Wnt signaling in thoracic malignancies", including mesothelioma and non small cell lung cancer. Chen et al. (2003) links Wnt signaling to melanoma progression. Miyoshi et al. (2002) teaches that Wnt expression induces mammary tumors.

Regarding Dkk-1 in particular, Wang et al. (2000) show that p53 exhibits its tumor suppressor activity through Dkk-1-mediated downregulation of the Wnt signaling pathway. In a mesothelioma model, Lee et al. (2004) show that Dkk-1 exerts a tumor suppressive effect by antagonizing Wnt signaling. Finally, Gonzalez-Sancho et al. (2005) teach, "Our data indicate that the Wnt/ β -catenin pathway is regulated by the induction of DKK-1 expression, a mechanism that is lost in colon cancer".

Clearly then, these combined teachings would not lead one of skill in the art to conclude that the downregulation of Dkk-1, causing the upregulation of Wnt, would be a good idea. While the specification provides some inconclusive teachings regarding the efficacy of a Dkk-1 antagonist for the treatment of insulin resistance or hypoinsulinemia, or the repair or regeneration of muscle, the prior art clearly teaches that the downregulation of Dkk-1, causing the upregulation of Wnt, would exacerbate, if not actually induce, any number of cancers - conditions far worse than the conditions the claimed method is intended to treat. Accordingly, it is the Examiner's position that the invention of the instant claims would require undue experimentation to practice as claimed.


5. No claim is allowed.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina

Art Unit: 1644

Chan can be reached on (571) 272-0841.

7. **Please Note:** Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


4/1/05

G.R. Ewoldt, Ph.D.
Primary Examiner
Technology Center 1600